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09/966,515	09/28/2001	Michael S. Kopreski	00-1312-C	5477

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[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1634

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10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/966,515	KOPRESKI, MICHAEL S.
	Examiner	Art Unit
	Frank W Lu	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 28 September 2001.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-53 is/are pending in the application.

4a) Of the above claim(s) 13-20,22-35,38,39,42-45 and 47-50 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-12,21,36,37,40,41,46 and 51-53 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) Z .

4) Interview Summary (PTO-413) Paper No(s). _____

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____

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DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-12, 21, 36, 37, and 40-53 and species of heterogeneous nuclear ribonucleoprotein A2/B1 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that: (1) "it would pose no undue burden on the Patent Office to search claims 13-15 and 22 (corresponding to Group II), 17-20 (group III), and 29-34, 38, and 39 (group V) with the elected claims." since "[T]he claims of all Groups are classified in class 435, subclass 91.2."; and "[T]he Patent Office will need to search class 435, subclass 92.1 with regard to the elected claims of Group I."

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the restriction requirement nor persuasive toward the relaxation of same such that Groups I, II, III, and V will be examined together. First, the restriction made on Groups I, II, III, and V in previous office action was not based on the classification of these Groups. Second, the examiner agreed with applicant "[T]he Patent Office will need to search class 435, subclass 92.1 with regard to the elected claims of Group I.". Although some searches for Groups I, II, III, and V may be identical, the searches for these groups are not coextensive. As shown in previous office action, different searches were required for Groups I, II, III, and V. Furthermore, MPEP 808.02 stated "[E]ven though they are classified together, each subject can be shown to have formed a separate subject for inventive effort when an explanation indicates a recognition of separate inventive effort by inventors. Separate status in the art may be shown by citing patents which are evidence of such separate status, and also of a separate field

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of search.”.

Therefore, the requirement is still deemed proper and is therefore made FINAL. Claims 1-12, 21, 36, 37, 40, 41, 46, and 51-53 will be examined.

Sequence Rules Compliance

2. The original filed sequencing listing has complied with Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Claim Objections

3. Claims 7 and 8 are objected to because of the following informalities: “an RNA” in line 2 should be “RNA”.

4. Claims 11 and 12 are objected to because of the following informalities: there is no period in the claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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7. Claim 21 is rejected as vague and indefinite because it is unclear whether step 1) is a method step or not. If step 1) is a method step, steps a) and b) of step 1) and step 1) do not correspond each other since it is impossible that a detection step [step 1)] includes a extraction step and an amplification step [steps a) and b)]. It appears that steps a) and (b) are not part of step 1). Please clarify.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-12, 21, 36, 37, 40, 41, 52, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kopreski *et al.*, (Clin. Cancer Res., 5, 1961-1965, August 1999) in view of Leitzel *et al.*, (Clin. Cancer Res., 4, 3037-3043, December 1998).

Note that, for the subject relating to epidermal growth factor receptor, the examiner considered that the priority date of this instant application was its filing date (September 28, 2001) since provisional application 60/014,730, PCT/US 97/03479, and US Patent No. 6,329,179 did not teach epidermal growth factor receptor.

Kopreski *et al.*, teach detection of tumor messenger RNA in the serum of patients with malignant melanoma.

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Regarding claims 1-6, 9-12, 21, 36, 37, 40, 41, 52, and 53, RNA isolated from sera (a bodily fluid recited in claim 2) of six patients (a human as recited in claims 11 and 12) with metastatic malignant melanoma treated on clinical protocols was used for RT-PCR of human tyrosinase cDNA. PCR products were detected by agarose gel electrophoresis or Southern Blot as recited in claims 5 and 6. The detection of tumor messenger RNA in the serum of patients indicated that the malignant or premalignant cells were present in the patient recited in claims 9 and 10 (see abstract, pages 1961-1963, and Figures 1-3). Although Kopreski *et al.*, did not directly disclose the limitations recited in claims 36, 37, 40, and 41, Kopreski *et al.*, did suggest that their method could be used in cancer diagnostics, monitoring, and pharmacogenomic evaluation recited in claims 36, 37, 40, and 41 (see left column in page 1964 and right column in page 1965).

Regarding claims 7 and 8, although Kopreski *et al.*, did not directly teach a RNA isolation method as recited in claims 7 and 8, these limitations were considered to be inherent to the reference taught by Kopreski *et al.*, since Kopreski *et al.*, taught isolation of RNA using a Total RNA Isolation Kit from 5 prime-3 Prime, Inc., which was used guanidine-thiocyanate-phenol solution extraction method.

Kopreski *et al.*, do not disclose the detection of epidermal growth factor receptor from sera or plasma from patients recited in claims 1, 2, and 21 and production of cDNA epidermal growth factor receptor from sera or plasma from patients recited in claims 52 and 53.

Leitzel *et al.*, teach detection of cancer cells in peripheral blood of breast cancer patients using reverse transcription-polymerase chain reaction for epidermal growth factor receptor. They

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suggested that RT-PCR for epidermal growth factor receptor was a sensitive and specific method for the detection of circulating micrometastases in a proportion of patients with metastatic breast cancer and the assay could be used to monitor the effectiveness of purging of breast cancer cells in patients undergoing high-dose chemotherapy and autologous bone marrow transplantation (see abstract in page 3037, page 3038, right column in page 3041, and left column in page 3042). This disclosure reasonably suggested that one having ordinary skill in the art at the time the invention was made would use this protein to monitor the effectiveness of various therapeutics and this protein would be used as a useful tool in monitoring a malignant or premalignant disease or response to an anticancer therapy, and performing a diagnostic test for diagnosing cancer or premalignancy as recited in claims 21, 36, 37, 40, and 41.

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have isolated total RNA from the plasma or serum or a bodily fluid and RT-PCR amplified RNA of epidermal growth factor receptor in view of the references from Kopreski *et al.*, and Leitzel *et al.*. One having ordinary skill in the art would have been motivated to modify the method of Kopreski *et al.*, and use the method of Kopreski *et al.*, to RT-PCR cDNA of epidermal growth factor receptor using total RNA isolated from patient sera because Kopreski *et al.*, suggested that other tumor mRNA could be demonstrated in serum and plasma in other malignancies using their method (see page left column in page 1965). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to RT-PCR of hTERT RNA isolated from patient sera.

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10. Claims 46 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou *et al.*, (J. Biol. Chem., 271, 10760-10766, May 1996) in view of Emanual *et al.*, (US Patent No. 5,576,178, filed on November 22, 1993).

Note that, for the subject relating to heterogeneous nuclear ribonucleoprotein A2/B1, the examiner considered that the priority date of this instant application was March 14, 1997, which was a filing date of PCT/US 97/03479 since provisional application 60/014,730 did not teach heterogeneous nuclear ribonucleoprotein A2/B1.

Zhou *et al.*, taught to RT-PCR amplify nuclear ribonucleoprotein splice forms A2 and B1 in the presence of primers (see page 805). They also taught reagents for extracting RNA (see right column in page 10761). Note that the examiner considered the method in the claims 46 and 51 as an intended use.

Zhou *et al.*, did not disclose a diagnostic kit

Emanual *et al.*, do teach a diagnostic kit comprising primers or probes (see abstract and column 24).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have organized oligonucleotides such as PCR primers taught by Zhou *et al.*, into a kit in view of prior art from Zhou *et al.*, and Emanuel *et al.*, because the kit format was utilized to not only assemble a variety of different reagents together but ensure the quality and compatibility of the reagents. One having ordinary skill in the art at the time the invention was made would have motivated to assemble reagent (s) of biotechnology methods into a kit in order to obtain the above discussed advantages,

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thus resulting in instant kit described in claims 46 and 51. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these prior art together because the kit could provide a convenient, efficient, economical way to practice the method of Zhou *et al.*.

11. Claims 46 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burd *et al.*, (Proc. Natl. Acad. Sci. USA, 86, 9788-9792, 1989) in view of Emanual *et al.*, (1993).

Burd *et al.*, teach cDNAs of heterogeneous nuclear ribonucleoprotein A2, B2, and C2 proteins and total RNA isolated from HeLa S3 cells. These cDNAs and total RNA were used in Northern Blot (see page 9788 and Figures 4 and 5). Note that: (1) although Burd *et al.*, did not directly show reagents for extracting RNA, this limitation was considered to be inherent to Burd *et al.*, since isolation of RNA required reagents for extracting RNA; and (2) the examiner considered the method in the claims 46 and 51 as an intended use.

Burd *et al.*, did not disclose a kit.

Emanual *et al.*, do teach a diagnostic kit comprising primers or probes (see abstract and column 24).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have organized cDNAs of heterogeneous nuclear ribonucleoprotein A2, B2, and C2 proteins, total RNA isolated from HeLa S3 cells and reagents for extracting RNA taught by Burd *et al.*, into a kit in view of prior art from Burd *et al.*, and Emanuel *et al.*, because the kit format was utilized to not only

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assemble a variety of different reagents together but ensure the quality and compatibility of the reagents. One having ordinary skill in the art at the time the invention was made would have motivated to assemble reagent (s) of biotechnology methods into a kit in order to obtain the above discussed advantages, thus resulting in instant kit described in claims 46 and 51. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these prior art together because the kit could provide a convenient, efficient, economical way to practice the method of Burd *et al.*, such as Northern Blot assay wherein cDNAs of heterogeneous nuclear ribonucleoprotein A2, B2, and C2 proteins and total RNA isolated from HeLa S3 cells were used.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-12, 21, 36, 37, 40, 41, 52, and 53 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim of U.S. Patent No. 6,229, 179B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims in this instant application is either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Note that, although claims 1-12, 21, 36, 37, 40, 41, 52, and 53 in this instant application are not identical to claims 1-24 of U.S. Patent No. 6,329, 179B1 and do not teach her-2/neu RNA, c-myc RNA, and heterogeneous nuclear ribonucleoprotein A2/B1 RNA, the limitations related to her-2/neu RNA, c-myc RNA, and heterogeneous nuclear ribonucleoprotein A2/B1 RNA were considered to be inherent to claims 1-24 of U.S. Patent No. 6,329, 179 B1 in light of disclosure of this patent since U.S. Patent No. 6,329, 179 B1 did teach RT-PCR of her-2/neu RNA, c-myc RNA, and heterogeneous nuclear ribonucleoprotein A2/B1 RNA (see column 11). Therefore, claims 1-24 of U.S. Patent No. 6,329, 179 B1 are directed to the same subject matter and fall entirely within the scope of claims 1-12, 21, 36, 37, 40, 41, 52, and 53 in this instant application.

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In other words, claims 1-12, 21, 36, 37, 40, 41, 52, and 53 in this instant application are anticipated by claims 1- 24 of U.S. Patent No.6,329, 179 B1.

Conclusion

14. No claim is allowed.
15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
November 6, 2002


ETHAN C. WHISENANT
PRIMARY EXAMINER